

NOVEL INFLUENZA

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description

Typical influenza symptoms include fever, headache, myalgia (body aches), prostration, coryza (runny nose), sore throat, and cough. However, variable symptoms, like conjunctivitis and bloody sputum, have been observed in cases caused by novel influenza viruses.

This disease plan will focus on two viruses of particular concern at this time: novel influenza A (H7N9) and variant influenza A (H3N2) (hereafter referred to as H7N9 and H3N2v).

Infection with H7N9 typically presents first with a high fever and cough. Many cases develop very serious illness, with complications including severe pneumonia, acute respiratory distress syndrome (ARDS), septic shock and multi-organ failure leading to death. Infection with H3N2v produces symptoms similar to seasonal influenza. The severity of H3N2v appears similar to seasonal influenza, as well.

Causative Agent

Influenza is caused by RNA viruses from the *Orthomyxoviridae* family. There are three types of influenza viruses: A, B, and C. Influenza A viruses are further categorized by their H (hemagglutinin) and N (neuraminidase) membrane glycoproteins.

Novel influenza viruses cause infection in a human with an influenza A virus subtype that is different from currently circulating human influenza H1 and H3 viruses. Novel subtypes include, but are not limited to, H2, H5, H7, and H9 subtypes. Influenza H1 and H3 subtypes originating from a non-human species or from genetic reassortment between animal and human viruses are also novel subtypes, although they are termed variant influenza viruses. Variant influenza viruses are a type of novel influenza virus.

Differential Diagnosis

Viruses that cause symptoms similar to influenza include: respiratory syncytial virus (RSV), adenovirus, parainfluenza, and human metapneumovirus.

Laboratory Identification

H7N9 and H3N2v infection cannot be definitively distinguished from seasonal influenza or other respiratory viruses clinically; thus laboratory confirmation is essential. It is essential for public health to be involved in all testing of novel influenza viruses to ensure that accurate results are obtained.

Culture

Viral culture should never be attempted if a patient is suspected to have a novel influenza virus.

RT-PCR

RT-PCR is the most sensitive method for influenza virus detection and the gold standard for influenza diagnosis. Most RT-PCR tests will be able to detect influenza A infection, but they will not be able to subtype the virus, and thus will not be able to indicate that the infection is a novel virus. Some RT-PCR tests will be able to subtype all currently circulating human influenza A subtypes, and thus a novel virus would be detected as an influenza A virus, with no subtype identified. These viruses should always be sent to UPHL for follow up testing.

Rapid Influenza Diagnostic Tests (RIDTs)

Rapid influenza diagnostic tests currently have unknown sensitivity and specificity for novel influenza virus infection. RIDTs are not recommended for detection of novel influenza viruses.

Utah Public Health Laboratory (UPHL) Testing

UPHL is capable of confirming H7N9, H5N1, and H3N2v influenza infection. For other novel influenza viruses, UPHL would detect an unsubtypeable influenza virus infection, and the specimen would be forwarded to CDC for further testing.

Additional information on specimen collection and testing for H3N2v and H7N9 can be found on the CDC website: [H3N2v specimen collection and testing](#) and [H7N9 specimen collection and testing](#).

Treatment

Patients with confirmed or suspected novel influenza virus infection can be treated with the same antivirals recommended for seasonal influenza (see the seasonal influenza disease investigation plan, or the CDC website: [Antiviral Drug Recommendations](#).) Because of the potential severity of illness associated with H7N9, antiviral treatment is recommended as soon as possible for all persons, including previously healthy persons. Treatment should be initiated even if it is more than 48 hours after onset of illness. Additional recommendations can be found on the CDC website: [Antiviral Drug Recommendations for H7N9](#).

Case Fatality

The case fatality rate for novel influenza viruses is variable, and could range from .01%, as is usually seen with seasonal influenza, to greater than 2.5%, as was seen with the 1918 influenza A (H1N1) pandemic. The case fatality rate for H3N2v appears similar to seasonal influenza, while the case fatality rate for laboratory confirmed H7N9 cases is 19%.

Reservoir

Many novel influenza viruses originate from animals, such as birds or pigs. The reservoir for H3N2v is pigs; the reservoir for H7N9 appears to be poultry in live bird markets.

Transmission

While human infection with avian influenza viruses is rare, it can occur after close contact with both live and dead infected birds, as well as environments contaminated with avian influenza virus. It is possible for poultry meat to be infected with avian influenza viruses; however, normal temperatures used for cooking will destroy the virus. Additionally, eggs

may also contain virus, both on the outside and inside. It is also possible for avian influenza viruses to be spread person-to-person, but this is very limited.

Human infection with swine influenza viruses is also rare, and typically occurs when a person inhales infected droplets created when an infected pig coughs or sneezes. Swine influenza viruses have not been shown to be transmitted to humans through pork meat. Like avian influenza, it is possible for swine influenza viruses to be transmitted person-to-person, but this is rare.

Susceptibility

Because novel influenza viruses typically lack the ability to easily spread from person-to-person, extensive transmission of the virus is usually limited. However, if a novel influenza virus mutates to spread from person-to-person efficiently, many people would become ill very quickly because very few people have antibodies against novel influenza viruses. In this situation, a large epidemic, or even global pandemic could occur.

Incubation Period

The incubation period for human influenza ranges from 1-4 days with an average of 2 days, however, novel influenza viruses may have a longer incubation period, up to 7-10 days.

Period of Communicability

Influenza patients (with typical human strains of influenza) can shed virus from 1 day prior to onset of symptoms until 3-5 days after onset, but can be transmitted up to 7 days after symptom onset in children. Immunocompromised persons can shed virus for weeks to months after infection.

Epidemiology

H3N2v infections have mostly been associated with prolonged exposure to pigs at agricultural fairs. Limited human-to-human spread of this virus has been detected in the past, but no sustained or community spread of H3N2v has been identified at this time. Many patients infected with H7N9 reported contact with poultry. The working assumption is that human infections occurred after exposure to infected poultry or contaminated environments. No evidence of sustained person-to-person spread of the H7N9 virus was found. To date, all cases of H7N9 have had exposure in China.

PUBLIC HEALTH CONTROL MEASURES

Public Health Responsibility

Public health's responsibility in regards to novel influenza viruses is threefold:

- **Early detection.** Public health should be monitoring circulating influenza A strains and conducting sufficient subtyping to be able to contribute to the national effort to detect novel influenza virus strains. Public health should also be communicating with clinicians to identify persons with compatible illness suspect for novel influenza, and ensuring that complete testing can be performed.
- **Rapid assessment and response.** Public health should respond to novel influenza cases quickly and implement necessary control measures to mitigate further exposure. Public health should report cases promptly to CDC and work with other government agencies to investigate the source of exposure.

- **Pandemic preparation.** Public health should have a robust plan developed to respond to an influenza pandemic that includes appropriate communication, surveillance, mitigation, and detection methods.

Prevention

“Respiratory etiquette” is another way to prevent infection, and includes:

- Staying away from people who are sick and staying away from other people when you are sick. Don’t go to work, school, church, or other places where people gather if you are sick.
- Covering your mouth and nose when you cough or sneeze. Use a disposable tissue and throw it away when you are done.
- Washing your hands with soap and warm water, or use alcohol-based hand sanitizers frequently.
- Avoid touching your eyes, nose, or mouth. Germs spread this way.
- Try to avoid close contact (e.g. within 6 feet) with sick people.
- If you get sick with influenza symptoms, CDC recommends that you stay home from work or school and limit contact with others to keep from infecting them.

Avian influenza viruses are destroyed by adequate heat, as are other foodborne pathogens. Consumers are reminded to follow proper food preparation and handling practices, including:

- Cook all poultry and poultry products (including eggs) thoroughly before eating. (This means that chicken should be cooked until it reaches a temperature of 180 degrees Fahrenheit, throughout each piece of chicken.)
- Raw poultry always should be handled hygienically because it can be associated with many infections, including salmonella. Therefore, all utensils and surfaces (including hands) that come in contact with raw poultry should be cleaned carefully with water and soap immediately afterwards.

For additional food safety issues, please see the WHO publication: [Avian Influenza: Food Safety Issues](#).

For those traveling to countries with avian influenza (H5N1) disease, please see the CDC publication: [Avian Influenza H7N9 in China](#).

Chemoprophylaxis

Because novel influenza viruses, including H7N9 and H3N2v, are usually not transmitted for person-to-person, chemoprophylaxis is not recommended. However, some individuals may receive chemoprophylaxis after consultation with physicians, the health department, and CDC.

Vaccine

No vaccine currently exists for novel influenza viruses. However, efforts to produce vaccine candidates that would be effective against H7N9 and H3N2v virus are under way.

Isolation and Quarantine

Voluntary Isolation

Symptomatic patients should not attend work or school if they are sick, and should stay away from public places to avoid further transmission. Persons who become ill with

influenza symptoms should stay at home for 7 days (this period could be longer depending on the novel influenza virus) after onset of symptoms, or for 24 hours after symptoms resolve, whichever is longer.

Healthcare Facilities

Infection control recommendations for H7N9 can be found in [CDC's Infection Control Within Healthcare Settings When Caring for Patients with Confirmed, Probable, or Cases Under Investigation of Avian Influenza A \(H7N9\) Virus Infection](#). Unless otherwise specified, other novel influenza virus cases can be managed by following CDC's [Influenza Infection Control in Health Care Facilities](#).

Quarantine: N/A.

✓ REPORTING

Novel influenza A cases are an immediately notifiable condition, both nationally and in Utah. Suspected cases of novel influenza A should be reported to public health, even before laboratory confirmation. Additionally, novel influenza is one of a few diseases immediately reportable to the World Health Organization (WHO) through the [International Health Regulations \(IHR\)](#).

Reporting Tables

Table of criteria to determine whether a case should be reported to public health authorities.

Criterion	Reporting		
<i>Clinical Evidence</i>			
Fever		O	N
Cough		O	O
Severe Pharyngeal Pain		O	O
<i>Laboratory Evidence</i>			
Non-subtypeable influenza A virus determined by WHO collaborating laboratory	S		
Influenza A, rapid diagnostic test			O
Influenza A, viral culture			O
Influenza A, RT-PCR			O
Influenza A H1			O
Influenza A H3			O
<i>Epidemiologic Evidence</i>			
Contact to a confirmed case of novel influenza virus infection		N	
Travel within 14 days to any country where a novel influenza A virus such as A(H5N1) has been identified in animals or people			O
Veterinarian			O
Works on a poultry farm			O
Works on a swine farm			O
Works in a poultry processing plant			O
Works in a swine processing plant			O
Works with wild birds			O
Contact with sick birds			O

Notes:

S = This criterion alone is Sufficient to identify a case for reporting.

N = All “N” criteria in the same column are Necessary to identify a case for reporting.

O = At least one of these “O” (Optional) criteria in each category (i.e., clinical evidence and laboratory evidence) in the same column—in conjunction with all “N” criteria in the same column—is required to identify a case for reporting. (These optional criteria are alternatives, which mean that a single column will have either no O criteria or multiple O criteria; no column should have only one O.)

Novel Influenza A Virus Infections (2010)

Case Definition

Clinical Description

An illness compatible with influenza virus infection (fever >100° Fahrenheit with cough or sore throat).

Laboratory Criteria for Diagnosis

A human case of infection with an influenza A virus subtype that is different from currently circulating human influenza H1 and H3 viruses. Novel subtypes include, but are not limited to, H2, H5, H7, and H9 subtypes. Influenza H1 and H3 subtypes originating from a non-human species or from genetic reassortment between animal and human viruses are also novel subtypes. Novel subtypes will be detected with methods available for detection of currently circulating human influenza viruses at state public health laboratories (e.g., real-time reverse transcriptase polymerase chain reaction [RTPCR]). Confirmation that an influenza A virus represents a novel virus will be performed by CDC’s influenza laboratory.

Exposure

Criteria for epidemiologic linkage:

- The patient has had contact with one or more persons who either have or had the disease,
AND
- Transmission of the agent by the usual modes of transmission is plausible
OR
- A case may be considered epidemiologically linked to a laboratory confirmed case if at least one case in the chain of transmission is laboratory confirmed

Case Classification

Cases Under Investigation

A case meeting the clinical criteria, pending laboratory confirmation. Any case of human infection with an influenza A virus that is different from currently circulating human influenza H1 and H3 viruses is classified as a suspected case until the confirmation process is complete.

Probable

A case meeting the clinical criteria and epidemiologically linked to a confirmed case, but for which no confirmatory laboratory testing for novel influenza virus infection has been performed.

Confirmed

A case of human infection with a novel influenza A virus confirmed by CDC's influenza laboratory. Once a novel virus has been identified by CDC, confirmation may be made by public health laboratories following CDC-approved protocols for that specific strain, or by laboratories using an FDA-authorized test specific for detection of that novel influenza strain.

Comment

Once a novel virus is identified by CDC, it will be nationally notifiable until CSTE in consultation with CDC determines that it is no longer necessary to report each case. On December 13, 2006, the United States formally accepted the [revision of the International Health Regulations, referred to as IHR \(2005\)](#). The [IHR \(2005\)](#) are an international legal instrument that governs the roles of the WHO and its member countries in identifying and responding to and sharing information about public health emergencies of international concern. The updated rules are designed to prevent and protect against the international spread of diseases, while minimizing interference with world travel and trade. The revised regulations add human infections with new influenza strains to the list of conditions that Member States must immediately report to WHO. An outbreak of infections with a new influenza A virus that demonstrates human-to-human transmission could signal the beginning of the next pandemic. Robust epidemiologic and laboratory surveillance systems are required for a coordinated public health response to infections with a novel influenza virus subtype. Early detection of an influenza virus with pandemic potential will permit identification of viral characteristics (i.e., genetic sequence, antiviral susceptibility, and virulence) that will affect clinical management and public health response measures. It should also facilitate development of a virus-specific vaccine and testing strategies.

All state public health laboratories have the capacity to test respiratory specimens for influenza viruses with sensitive and specific assays that can detect human and non-human influenza A viruses. They also have the capacity to subtype currently circulating human influenza A H1, H3, and avian H5 (Asian lineage) viruses. The detection or confirmation by a state public health laboratory of an influenza A virus that is unsubtypeable with standard methods (e.g., real-time RT-PCR assays for human influenza A(H3) or (H1) viruses), or a non-human influenza virus (e.g., H5) from a human specimen, could be the initial identification of a virus with pandemic potential. Prompt notification of CDC by a state epidemiologist in conjunction with the public health laboratory will permit rapid confirmation of results and reporting to WHO. In addition, it will aid prompt viral characterization, and the development of virus-specific diagnostic tests.

Classification Table

Criteria for defining a novel influenza A virus infection.

Criterion	Case Definition		
	Confirmed	Probable	Case Under Investigation
<i>Clinical Evidence</i>			
Fever		N	N
Cough		O	O
Headache		O	O
Myalgia		O	O
Severe Pharyngeal Pain		O	O

<i>Laboratory Evidence</i>			
Novel influenza A virus confirmed by CDC's influenza laboratory	S		
Laboratory test to confirm novel influenza A virus pending			N
<i>Epidemiologic Evidence</i>			
Contact to a confirmed case of novel influenza virus infection		N	

Novel Influenza A (H7N9)

Confirmed Case

Avian influenza A (H7N9) virus infection in a patient that is confirmed by CDC's Influenza Laboratory or a CDC certified public health laboratory using methods agreed upon by CDC and CSTE. Confirmation of avian influenza A (H7N9) viruses may be made by public health laboratories following CDC-approved protocols for detection of avian influenza A (H7N9) virus, or by laboratories using an FDA-authorized test specific for detection of avian influenza A (H7N9) virus.

Probable Case

Illness compatible with influenza in a patient meeting any of the exposure criteria below and for whom laboratory diagnostic testing is positive for influenza A, negative for H1, negative for H1pdm09, and negative for H3 by real-time reverse transcription polymerase chain reaction (RT-PCR) and therefore unsubtypeable.

Case Under Investigation

Illness compatible with influenza in a patient meeting any of the exposure criteria below and for whom laboratory confirmation is not known or pending or for whom test results do not provide a sufficient level of detail to confirm avian influenza A (H7N9) virus infection.

Exposure Criteria

- Patients with recent travel (within <10 days of illness onset) to areas where human cases of avian influenza A (H7N9) virus infection have become infected or to areas where avian influenza A (H7N9) viruses are known to be circulating in animals. As of June 3, 2013, China was the only country where avian influenza A (H7N9) viruses were known to be circulating in animals or where human cases have become infected.

OR

- Patients who have had recent close contact (within <10 days of illness onset) with confirmed cases of human infection with avian influenza A (H7N9) virus. Close contact may be regarded as coming within about 6 feet (2 meters) of a confirmed case while the case was ill (beginning 1 day prior to illness onset and continuing until resolution of illness). This includes healthcare personnel providing care for a confirmed case, family members of a confirmed case, persons who lived with or stayed overnight with a confirmed case, and others who have had similar close physical contact.

Variant Influenza A (H3N2v)

Confirmed

Influenza A (H3N2)v virus infection in a patient with laboratory confirmation by:

- Reverse-transcription polymerase chain reaction (RT-PCR) testing or genetic sequencing results positive for influenza A (H3N2)v virus at the CDC Influenza Division Laboratory
- OR
- RT-PCR testing results at a public health laboratory consistent with influenza A (H3N2)v virus using a CDC-approved assay (for example, InfA, H3, and pdmInfA positive results, and H1 and pdmH1 negative results using the CDC Flu rRT-PCR Dx Panel).

Case Under Investigation

Illness compatible with influenza in a patient meeting at least one of the epidemiologic criteria below for whom laboratory confirmation is not known or pending, or for whom test results do not provide a sufficient level of detail to confirm influenza A (H3N2)v virus (e.g., a positive rapid influenza diagnostic test). Illness compatible with influenza may present as influenza-like illness (ILI) [fever $\geq 100^{\circ}\text{F}$ plus cough or sore throat]. Note that influenza may not cause fever in all patients (especially in patients under 5 years of age, over 65 years of age, or patients with immune-suppression), and the absence of fever should not supersede clinical judgment when evaluating a patient for illness compatible with influenza.

Exposure Criteria

- Recent close contact (within 7 days of illness onset) with confirmed cases of influenza A (H3N2)v virus infection
- OR
- Recent contact (within 7 days of illness onset) with swine or recent attendance at an event (such as an agricultural fair) where swine were present. Contact with swine may be direct contact (i.e., touching or handling a pig) or indirect contact (coming within about 6 feet (2 meters) of a pig without known direct contact).

✓CASE INVESTIGATION

Case Investigation Process

H7N9

Patients who meet both the clinical and exposure criteria described below should be considered for H7N9 testing by reverse-transcription polymerase chain reaction (RT-PCR) methods. Decisions on diagnostic testing for influenza using RT-PCR should be made using available clinical and epidemiologic information, and additional persons in whom clinicians suspect H7N9 infection should also be tested.

Clinical Illness Criteria

- Patients with new-onset severe acute respiratory infection requiring hospitalization (i.e., illness of suspected infectious etiology that is severe enough to require inpatient medical care in the judgment of the treating clinician).
- AND
- Patients for whom no alternative infectious etiology is identified.

Exposure Criteria

- Patients with recent travel (within 10 days of illness onset) to areas where human cases of H7N9 have become infected or to areas where avian influenza A (H7N9) viruses are known to be circulating in animals. As of June 3, 2013, China is the only country where H7N9 viruses were known to be circulating in animals or where human cases have become infected. Patients with direct or close contact with wild birds or poultry, or animal settings, such as live poultry markets while traveling in these areas should be strongly considered for H7N9 testing.
- OR
- Patients who have had recent close contact of a confirmed case.

H3N2v

Patients who meet both the clinical and exposure criteria described below should be considered for H3N2v testing by reverse-transcription polymerase chain reaction (RT-PCR) methods.

Clinical Illness Criteria

- Illness compatible with influenza in a patient for whom laboratory confirmation is not known or pending, or for whom test results do not provide a sufficient level of detail to confirm influenza A (H3N2)v virus (e.g., a positive rapid influenza diagnostic test). Patients with illness compatible with influenza may present as influenza-like illness (ILI) [fever $\geq 100^{\circ}\text{F}$ plus cough or sore throat]. Note that influenza may not cause fever in all patients (especially in patients under 5 years of age, over 65 years of age, or patients with immune-suppression), and the absence of fever should not supersede clinical judgment when evaluating a patient for illness compatible with influenza.

Exposure Criteria

- Recent close contact with confirmed cases of influenza A (H3N2)v virus infection
- OR
- Recent contact (within 7 days of illness onset) with swine or recent attendance at an event (such as an agricultural fair) where swine were present. Contact with swine may be direct contact (i.e., touching or handling a pig) or indirect contact (coming within about 6 feet (2 meters) of a pig without known direct contact).

Outbreaks

There have been no outbreaks in humans due to sustained human-to-human transmission of either H7N9 or H3N2v. H3N2v infections have mostly been associated with prolonged exposure to pigs at agricultural fairs. Limited human-to-human spread of this virus has been detected in the past, but no sustained or community spread of H3N2v has been identified at this time. Many patients infected with H7N9 reported contact with poultry. The working assumption is that human infections occurred after exposure to infected poultry or contaminated environments. No evidence of sustained person-to-person spread of the H7N9 virus was found.

Case Contacts

Identification

All close contacts of novel influenza cases should be identified. Close contact may be regarded as coming within about 6 feet (2 meters) of a confirmed case. For H3N2v the time frame should be within 7 days of illness onset through resolution of illness, for H7N9 the time frame should be within 10 days of illness onset through resolution of illness. This includes healthcare personnel providing care for a confirmed case, family members of a confirmed case, persons who lived with or stayed overnight with a confirmed case, and others who have had similar close physical contact.

Management

Management of close contacts should follow CDC guidelines.

REFERENCES

CDC's Avian Influenza A (H7N9) Website. <http://www.cdc.gov/flu/avianflu/index.htm>.

CDC's Influenza A (H3N2) Variant Virus Website. <http://www.cdc.gov/flu/swineflu/h3n2v-cases.htm>.

WHO's Avian Influenza A (H7N9) Website.
http://www.who.int/influenza/human_animal_interface/influenza_h7n9/en/index.html.

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